



THE UNIVERSITY *of* EDINBURGH

Edinburgh Research Explorer

Improved dynamics and positional bias with a second generation palladium(II)-complexed molecular shuttle

Citation for published version:

Leigh, DA, Lusby, PJ, McBurney, RT & Symes, MD 2010, 'Improved dynamics and positional bias with a second generation palladium(II)-complexed molecular shuttle', *Chemical Communications*, vol. 46, no. 14, pp. 2382-2384. <https://doi.org/10.1039/c001697g>

Digital Object Identifier (DOI):

[10.1039/c001697g](https://doi.org/10.1039/c001697g)

Link:

[Link to publication record in Edinburgh Research Explorer](#)

Document Version:

Peer reviewed version

Published In:

Chemical Communications

Publisher Rights Statement:

Copyright © 2010 by the Royal Society of Chemistry. All rights reserved.

General rights

Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy

The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact openaccess@ed.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.



Post-print of a peer-reviewed article published by the Royal Society of Chemistry.

Published article available at: <http://dx.doi.org/10.1039/C001697G>

Cite as:

Leigh, D. A., Lusby, P. J., McBurney, R. T., & Symes, M. D. (2010). Improved dynamics and positional bias with a second generation palladium(II)-complexed molecular shuttle. *Chemical Communications*, 46(14), 2382-2384.

Manuscript received: 27/01/2010; Accepted: 22/02/2010; Article published: 05/03/2010

Improved dynamics and positional bias with a second generation palladium(II)-complexed molecular shuttle**

David A. Leigh,^{1,*} Paul J. Lusby,^{1,*} Roy T. McBurney¹ and Mark D. Symes¹

^[1]EaStCHEM, School of Chemistry, Joseph Black Building, University of Edinburgh, West Mains Road, Edinburgh, EH9 3JJ, UK.

^[*]Corresponding authors; D.A.L. e-mail: David.Laigh@ed.ac.uk; P.J.L. e-mail: Paul.Lusby@ed.ac.uk; fax: +44 (0)131-650-6453

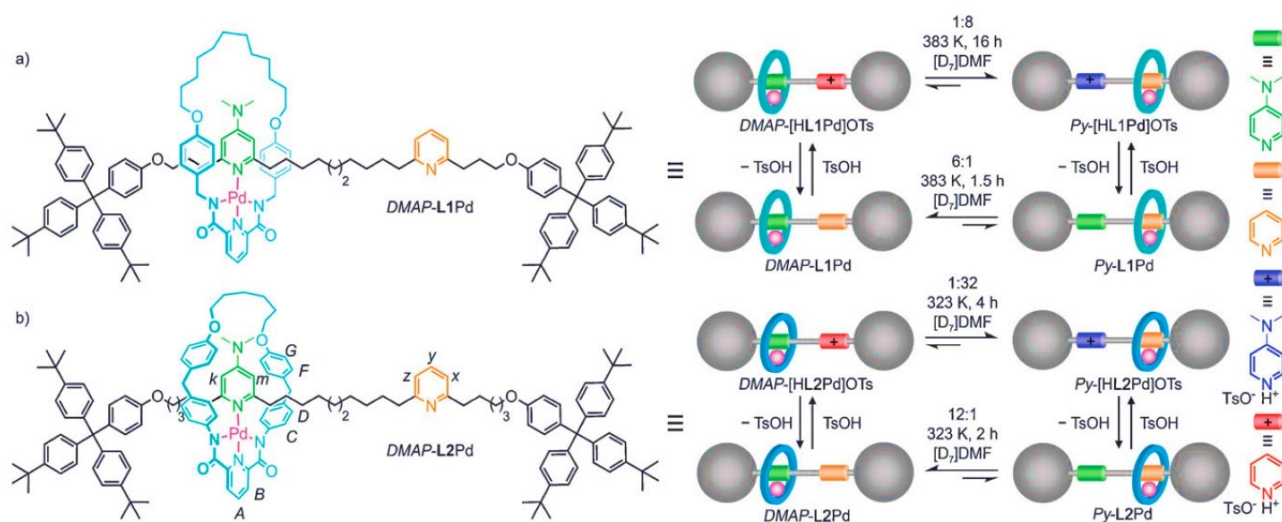
^[**]We thank Marika de Cremoux for assistance with the high field ¹³C NMR experiments and the EPSRC National Mass Spectrometry Service Centre (Swansea, UK) for accurate mass data. This work was supported by the EPSRC. P.J.L. is a Royal Society University Research Fellow. D.A.L. is an EPSRC Senior Research Fellow and holds a Royal Society-Wolfson Research Merit Award.

Supporting information:

^[†]Electronic Supplementary Information (ESI) available: Synthesis and characterisation of all compounds. See <http://dx.doi.org/10.1039/C001697G>

A second generation palladium(II)-complexed molecular shuttle, featuring structural changes to the size and shape of the macrocycle, shows significantly increased rates of shuttling and improved co-conformational bias compared to the original system.

An understanding of how structural variations affect the positional bias and the kinetics of shuttling is important for developing rotaxane systems that possess a level of control over motion beyond that of simple switches.¹ We recently described the synthesis and dynamics of a pH-responsive Pd(II)-complexed molecular shuttle² **L1Pd** (Scheme 1a)—only the second class of rotaxane system (following Sauvage’s use of Cu(I) and Cu(II)/Zn(II))³ in which co-conformational switching is dependent upon the energetics of metal-ligand coordination. A notable feature of rotaxane **L1Pd** was its metastability; changing the chemical state of the thread did not immediately cause a change in the macrocycle’s position. Whilst this allowed the system to be held in an out-of-equilibrium state—something that is difficult⁴ to achieve using molecular shuttles that rely on weaker non-covalent interactions⁵—elevated temperatures and extended times were required to overcome the energy barrier to shuttling (up to 16 hours at 383 K to reach equilibrium²). Furthermore, the positional bias of the Pd-macrocycle between the 4-dimethylaminopyridine (*DMAP*) and pyridine (*Py*) stations was somewhat modest in both the neutral (*ca.* 6:1) and protonated (*ca.* 1:8) states of the rotaxane thread (Scheme 1a).

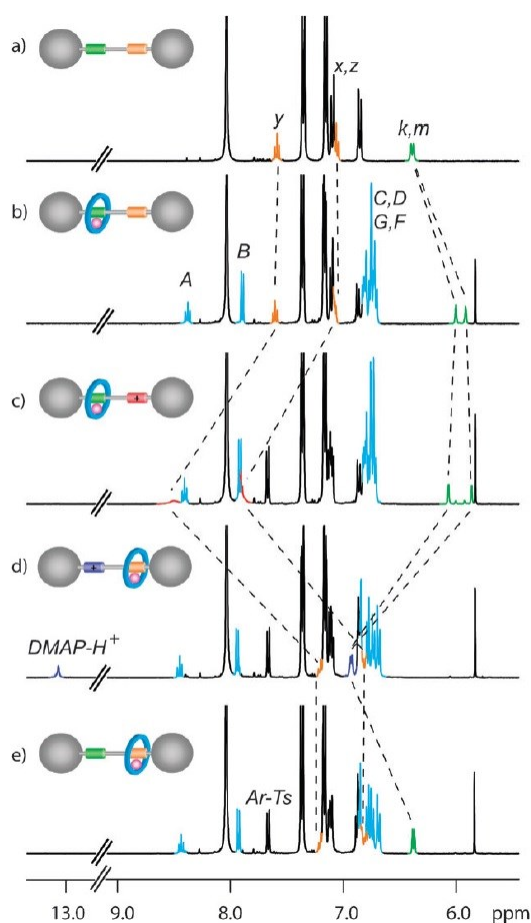


Scheme 1. Operation conditions and positional bias of (a) 1st generation² L1Pd and (b) 2nd generation L2Pd molecular shuttles.

Here we report on a second generation molecular shuttle, **L2Pd** (Scheme 1b), in which the benzylic amide macrocycle is replaced by a larger and differently shaped *bis*-anilide ring.⁶ The alteration of the steric environment around the palladium(II) centre in the rotaxane leads to greatly enhanced rates of macrocycle shuttling and improved positional bias in both chemical states of the thread. In addition to the minimum energy co-conformers of the two switched systems, two metastable out-of-equilibrium positional isomers were sufficiently stable to be isolated and characterised by ¹H NMR spectroscopy.

L2Pd was prepared by a threading-and-stoppering procedure,⁷ first treating a palladium-macrocycle-acetonitrile complex⁶ with an unstoppered-*DMAP*-end thread precursor, and the resulting pseudo-rotaxane reacted with an excess of a phenol-based stopper under Mitsunobu conditions to afford the [2]rotaxane (see Supporting Information).

Comparison of the ¹H NMR spectra of the free thread (Figure 1a) and the rotaxane isolated from the stoppering reaction (Figure 1b) showed that the signals assigned to the *DMAP* station (H_k and H_m) were split and shifted upfield by around 0.4 ppm in the rotaxane. In contrast, those of the *Py* station (H_x , H_y and H_z) were unchanged relative to their positions in the free thread, indicating that the co-conformation of the isolated [2]rotaxane was *DMAP-L2Pd*,⁸ i.e. with the palladium-macrocycle component coordinated to the *DMAP* station.



← **Figure 1.** ¹H NMR spectra (400 MHz, [D₇]DMF, 300 K) of [2]rotaxane [**L2Pd**] in four different protonated and co-conformational states and, for comparison, the free thread. a) Thread; b) *DMAP*-[**L2Pd**]; c) *DMAP*-[**HL2Pd**]OTs; d) *Py*-[**HL2Pd**]OTs (97% + 3% *DMAP*-[**HL2Pd**]OTs); e) *Py*-[**L2Pd**] (97% + 3% *DMAP*-[**L2Pd**]). The lettering in the figure refers to the assignments in Scheme 1.

Addition of one equivalent of *p*-toluenesulfonic acid (TsOH) to *DMAP-L2Pd* in [D₇]DMF gave *DMAP*-[downfield shifting of the signals associated with the protonated *Py* station -[HL2Pd]OTs, evidenced (Figure 1c) by broadening and (*H_y* by 0.9 ppm and *H_x* and *H_z* each by ~0.8 ppm). The positions of the *DMAP* unit peaks (*H_k* and *H_m*) were virtually unchanged relative to *DMAP-L2Pd* (Figure 1b).

After one hour at room temperature in [D₇]DMF, small changes to the ¹H NMR spectrum of this sample gave an indication that the activation barrier to macrocycle movement in the second generation molecular shuttle was significantly lower than for *DMAP*-[HL1Pd]OTs,² and after four hours at 323 K a new equilibrium co-conformation had been fully realised (i.e. no further spectral changes were observed). The ¹H NMR now showed (Figure 1d) a protonated *DMAP* signal at around 13 ppm for the major positional isomer present, shielding of the pyridine station signals (*H_x*, *H_y* and *H_z*) and a downfield shift of the *DMAP* heterocyclic signals (*H_k* and *H_m*), all of which indicated that the Pd-macrocycle was now bound to the pyridine station and a proton to the *DMAP* site. Integration indicated that the distribution of co-conformers at equilibrium was ~3:97 *DMAP:Py*-[HL2Pd]OTs. Deprotonation of the dimethylaminopyridinium group by addition of Na₂CO₃ gave an out-of-equilibrium co-conformational mixture of ~3:97 *DMAP:Py-L2Pd*, apparent through changes to the ¹H NMR spectrum (Figure 1e) the most noticeable of which were a return of the *DMAP* signals (*H_k* and *H_m*) to positions similar to those of the free thread (Figure 1a) and the disappearance of the protonated *DMAP* signal at 13 ppm. Again, slow isomerisation of the sample (~5% an hour) was observed at room temperature in [D₇]DMF but not in non-coordinating solvents such as CDCl₃, supporting a solvent-mediated switching mechanism for translocation of the Pd-coordinated macrocycle between the *Py* and *DMAP* units. Raising the temperature to 323 K in [D₇]DMF brought about the energetically downhill shuttling of the Pd-macrocycle from the *Py* to the *DMAP* station, yielding an equilibrium ratio of 92:8 *DMAP:Py-L2Pd* after just 2 hours.

The associative nature of palladium(II) substitution reactions, and the faster shuttling rate of **L2Pd** compared to **L1Pd**, suggests that the *bis*-anilide macrocycle provides a less sterically demanding environment around the metal ion and thus easier access for an incoming coordinating solvent molecule or TsO[−] counter-anion. In the protonated state, the better positional bias of [HL2Pd]⁺ with respect to [HL1Pd]⁺ suggests that the Pd-(*bis*-anilide) macrocycle binds less strongly to the track than the Pd-(benzylic amide) component (the relative p*K_a*'s of the protonated stations dominate the co-conformational energetics of [HL2Pd]⁺). This weaker interaction might also result in a longer Pd-N(thread) bond and increased access to the metal centre, which would also be consistent with the lower activation barrier to shuttling. Whilst the weakening of this interaction might be expected to produce a poorer co-conformational bias in the absence of acid, in fact the bias for **L2Pd** is 12:1 *DMAP:Py* in comparison to 6:1 for **L1Pd** (Schemes 1a and 1b). The reasons for the rather counter-intuitive improved positional discrimination in this neutral state of the thread are probably a subtle balance of solvation, metal-ligand coordination and π-stacking effects.

In conclusion, we have described a second generation pH-switchable Pd(II)-complexed molecular shuttle which shows significantly increased rates of shuttling compared to the first generation system and also exhibits better positional discrimination of the macrocycle, somewhat surprisingly, in both chemical states of the rotaxane thread. The improved level of control should prove useful for the development of switchable, metastable, components for advanced molecular machinery, including Brownian ratchets¹ and synthetic molecular walkers⁹.

Notes and references

- [1] E. R. Kay, D. A. Leigh and F. Zerbetto, *Angew. Chem. Int. Ed.* 2007, **46**, 72-191.
- [2] J. D. Crowley, D. A. Leigh, P. J. Lusby, R. T. McBurney, L.-E. Perret-Aebi, C. Petzold, A. M. Z. Slawin and M. D. Symes, *J. Am. Chem. Soc.* 2007, **129**, 15085-15090.
- [3] See, for example, A. Livoreil, C. O. Dietrich-Buchecker and J.-P. Sauvage, *J. Am. Chem. Soc.* 1994, **116**, 9399-9400; D. J. Cárdenas, A. Livoreil and J.-P. Sauvage, *J. Am. Chem. Soc.* 1996, **118**, 11980-11981; A. Livoreil, J.-P. Sauvage, N. Armaroli, V. Balzani, L. Flamigni and B. Ventura, *J. Am. Chem. Soc.* 1997, **119**, 12114-12124; N. Armaroli, V. Balzani, J.-P. Collin, P. Gaviña, J.-P. Sauvage and B. Ventura, *J. Am. Chem. Soc.* 1999, **121**, 4397-4408; F. Durola and J.-P. Sauvage, *Angew. Chem. Int. Ed.* 2007, **46**, 3537-3540; G. Periyasamy, J.-P. Collin, J.-P. Sauvage, R. D. Levine and F. Remacle, *Chem. Eur. J.* 2009, **15**, 1310-1313; F. Durola, J. Lux and J.-P. Sauvage, *Chem. Eur. J.* 2009, **15**, 4124-4134; J.-P. Collin, F. Durola, J. Lux and J.-P. Sauvage, *Angew. Chem. Int. Ed.* 2009, **47**, 8532-8535.
- [4] M. N. Chatterjee, E. R. Kay and D. A. Leigh, *J. Am. Chem. Soc.* 2006, **128**, 4058-4073; V. Serreli, C.-F. Lee, E. R. Kay and D. A. Leigh, *Nature* 2007, **445**, 523-527; M. Alvarez-Pérez, S. M. Goldup, D. A. Leigh and A. M. Z. Slawin, *J. Am. Chem. Soc.* 2008, **130**, 1836-1838.
- [5] For recent articles on molecular shuttles that exploit weak non-covalent interactions, see: S. Angelos, N. M. Khashab, Y.-W. Yang, A. Trabolsi, H. A. Khatib, J. F. Stoddart and J. I. Zink, *J. Am. Chem. Soc.* 2009, **131**, 12912-12914; L. Fang, M. Hmadeh, J. Wu, M. A. Olson, J. M. Spruell, A. Trabolsi, Y.-W. Yang, M. Elhabri, A.-M. Albrecht-Gary and J. F. Stoddart, *J. Am. Chem. Soc.* 2009, **131**, 7126-7134; A. Moretto, I. Menegazzo, M. Crisma, E. J. Shotton, H. Nowell, S. Mammi and C. Toniolo, *Angew. Chem. Int. Ed.* 2009, **47**, 8986-8989; F.-Y. Ji, L.-L. Zhu, D. Zhang, Z.-F. Chen and H. Tian, *Tetrahedron* 2009, **65**, 9081-9085; F. Coutrot and E. Busseron, *Chem. Eur. J.* 2009, **15**, 5186-5190; F.-Y. Ji, L.-L. Zhu, X. Ma, Q.-C. Wang and H. Tian, *Tetrahedron Lett.* 2009, **50**, 597-600; C.-J. Chuang, W.-S. Li, C.-C. Lai, Y.-H. Liu, S.-M. Peng, I. Chao and S.-H. Chiu, *Org. Lett.*, 2009, **11**, 385-388; C.-F. Lee, D. A. Leigh, R. G. Pritchard, D. Schultz, S. J. Teat, G. A. Timco and R. E. P. Winpenny, *Nature* 2009, **458**, 314-318; Y. Makita, N. Kihara and T. Takata, *J. Org. Chem.* 2008, **73**, 9245-9250; T. Umehara, H. Kawai, K. Fujiwara and T. Suzuki, *J. Am. Chem. Soc.* 2008, **130**, 13981-13988; M. J. Barrell, D. A. Leigh, P. J. Lusby and A. M. Z. Slawin, *Angew. Chem. Int. Ed.* 2008, **47**, 8036-8039; J. Berná, S. M. Goldup, A.-L. Lee, D. A. Leigh, M. D. Symes, G. Teobaldi and F. Zerbetto, *Angew. Chem. Int. Ed.* 2008, **47**, 4392-4396; V. Aucagne, J. Berná, J. D. Crowley, S. M. Goldup, K. D. Haenni, D. A. Leigh, P. J. Lusby, V. E. Ronaldson, A. M. Z. Slawin, A. Viterisi and D. B. Walker, *J. Am. Chem. Soc.* 2007, **129**, 11950-11963. For recent review articles highlighting various aspects of molecular shuttles, see: J. F. Stoddart, *Chem. Soc. Rev.* 2009, **38**, 1802-1820; P. Bodis, M. R. Panman, B. H. Bakker, A. Mateo-Alonso, M. Prato, W. J. Buma, A. M. Brouwer, E. R. Kay, D. A. Leigh and S. Woutersen, *Acc. Chem. Res.* 2009, **42**, 1462-1469;

- J. D. Crowley, S. M. Goldup, A.-L. Lee, D. A. Leigh and R. T. McBurney, *Chem. Soc. Rev.* 2009, **38**, 1530-1541; S. Silvi, M. Venturi and A. Credi, *J. Mater. Chem.* 2009, **19**, 2279-2294.
- [6] S. M. Goldup, D. A. Leigh, P. J. Lusby, R. T. McBurney and A. M. Z. Slawin, *Angew. Chem. Int. Ed.* 2008, **47**, 3381-3384.
- [7] D. B. Amabilino and J. F. Stoddart, *Chem Rev.* 1995, **95**, 2725-2828.
- [8] The italicised prefix (*DMAP*- or *Py*-) refers to the position of the macrocycle in the rotaxane.
- [9] M. von Delius, E. M. Geertsema and D. A. Leigh, *Nature Chem.* 2010, **2**, 96-101.